

**Amendments to the Claims:**

The listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

1. (original) A method for determining depth of a volume comprising a fluorophore in a turbid medium using time domain(TD) optical fluorescence, said method comprising:
  - i) obtaining at least one temporal point spread function (TPSF) by injecting light at an injection point at an excitation wavelength of said fluorophore and detecting light at a detection point at an emission wavelength of said fluorophore;
  - ii) determining a time  $t_{\max}$  substantially corresponding to the maximum of said TPSF;
  - iii) correlating said  $t_{\max}$  with said depth to determine the depth, and wherein said depth is insensitive to fluorophore concentration.
2. (original) The method as claimed in claim 1 wherein said step of correlating comprises:
  - a) establishing a calibration curve of  $t_{\max}$  as a function of depth for a plurality of depths;
  - b) using said calibration curve and said  $t_{\max}$  determined in step ii) to obtain said depth of said volume.
3. (original) The method as claimed in claim 1 wherein said injection and detection points are in a backreflection geometry.
4. (original) The method as claimed in claim 3 wherein said injection and detection points are substantially equidistant from said volume.

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5. (original) The method as claimed in claim 4 wherein said step of correlating comprises:

- a) providing scatter coefficient, speed of light in said medium and a lifetime of said fluorophore in said medium;
- b) calculating said depth using said  $t_{\max}$  and said scatter coefficient, said speed of light and said lifetime.

6. (currently amended) The method as claimed in claim ~~4~~ or 5 further comprising a step of estimating a position of said fluorophore in a plane substantially perpendicular to said depth prior to said step of obtaining said TPSF.

7. (original) The method as claimed in claim 6 wherein said step of estimating is performed by obtaining a topographic image of a region of interest containing said fluorophore.

8. (currently amended) The method as claimed in ~~any one of~~ claims 1 -7 wherein said fluorophore is an intrinsic or extrinsic fluorophore.

9. (currently amended) The method as claimed in ~~any one of~~ claim 5-8 wherein said scatter coefficient and lifetime are obtained using time domain optical measurements of said medium.

10. (currently amended) The method as claimed in ~~any one of~~ claim 5-8 wherein said scatter coefficient, lifetime and speed of light are obtained by matching said medium with a similar medium in a database for which optical properties are known.

11. (currently amended) The method as claimed in ~~any one of~~ claim 5-10, wherein said scatter coefficient and said speed of light are substantially the same at both the excitation or emission wavelength of the fluorophore and are determined at either said emission or said excitation wavelength.

12. (currently amended) The method as claimed in ~~any one of claim 5-10~~, wherein said scatter coefficient and said speed of light are determined at the fluorophore excitation and emission wavelength.

13. (currently amended) A method for estimating concentration of a fluorophore in a volume in a turbid medium using optical fluorescence, said method comprising:

- i) obtaining depth of said volume using the method ~~of any one of claim 1-12~~;
- ~~iii)~~ ii) obtaining a fluorescence emission Intensity of said fluorophore; and
- ~~iv)~~ iii) deriving said concentration from a fluorescence emission equation.

14. (original) The method as claimed in claim 13 wherein said emission intensity is obtained in a back-reflection configuration.

15. (original) The method as claimed in claim 13 wherein said fluorescence emission intensity is obtained in a trans-illumination configuration.

16. (currently amended) The method as claimed in claim 14 ~~or 15~~ wherein said emission intensity is obtained in a modality selected from time domain, frequency domain and continuous wave.

17. (currently amended) The method as claimed in ~~any one of claim 13-16~~ wherein said equation provides concentration of a fluorophore as a function of depth, scatter coefficient and absorption coefficient.

18. (original) The method as claimed in claim 17 wherein said coefficients are obtained using time domain optical measurements of said medium.

19. (original) The method as claimed in claim 17 wherein said coefficients are obtained by matching said medium with a similar medium from a database for which the optical properties are known.

20. (currently amended) The method as claimed in ~~any one of~~ claim 17-19, wherein said coefficients are substantially the same at both the excitation or emission wavelength of the fluorophore and is determined at either said emission or said excitation wavelength.

21. (currently amended) The method as claimed in ~~any one of~~ claim 17-19, wherein said at least one optical property is determined at the fluorophore excitation and emission wavelength.

22. (currently amended) The method as claimed in ~~any one of~~ claim 13-24 wherein said concentration is a relative concentration.

23. (currently amended) The method as claimed in ~~any one of~~ claim 13-24 wherein said concentration is an absolute concentration derived by calibrating said intensity.

24. (currently amended) A method for generating a tomographic image of a fluorophore distribution in a turbid medium said method comprising:

- i) obtaining a topographic image of said fluorophore distribution;
- ii) determining depth of a plurality of volumes of interest comprising said fluorophore using the method as claimed in ~~any one of~~ claim 1-12;
- iii) combining said depth information and said topographic image to generate a tomographic image of said distribution.

25. (currently amended) The method as claimed in claim 24 wherein said tomographic image is further processed with the method as claimed in ~~any one of~~ claim

13-23 to generate a tomographic fluorophore concentration image.

26. (currently amended) A method for determining a relative or absolute concentration of a fluorophore in a turbid medium said method comprising:

- i) establishing a calibration curve relating an emission intensity measurement in said turbid medium and concentration and depth of said fluorophore;
- ii) determining a depth of said fluorophore using the method as claimed in ~~any one of claim 1-12~~; and
- iii) determining said concentration using said calibration curve.

27. (currently amended) The method as claimed in ~~any one of claims 1-26~~ wherein time domain information is obtained by acquiring Frequency Domain (FD) data and applying a Fourier Transform to said data.

28. (original) An apparatus for determining depth and concentration of a fluorophore in a turbid medium comprised within an object, said apparatus comprising:

- a light source, optically coupled to a source channel and said object, to inject light in said object at a desired point and excitation wavelength;
- a first detector channel, optically coupled to a photon detector and said object, in a backreflection geometry relative to said source channel, to acquire at least one temporal point spread function from a desired point of said object to determine depth of said fluorophore;
- a second detector channel in a trans-illumination geometry relative to said source channel, to measure an emission intensity of said fluorophore;
- a means for spatially positioning said object relative to said channels;

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a depth calculator; and  
a concentration calculator.

29. (original)        The apparatus as claimed in claim 28 wherein said source and detector channels are in a configuration selected from contact and free-space optic.

30. (currently amended)    The apparatus as claimed in claim 28 ~~or 29~~ wherein said channels comprise optical coupling means selected from, mirrors, optic fibers.

31. (currently amended)    The apparatus as claimed in ~~any one of~~ claim 28-30 wherein said channels are mounted in a fixed position relative to one another.

32. (currently amended)        The apparatus as claimed in claim ~~34~~ 28 wherein said channels are mounted on a gantry that is moveable relative to said object.

33. (currently amended)    The apparatus as claimed in ~~any one of~~ claim 28-30 wherein said channels are independently moveable.

34. (currently amended)    The apparatus as claimed in ~~any one of~~ claim 30-33 28 wherein said object is placed on a platform transparent to an emission wavelength.

35. (currently amended)        The apparatus as claimed in claim ~~35~~ 34 wherein said platform is moveable relative to said channels.

36. (currently amended)    The apparatus as claimed in ~~any one of~~ claim 28-35 wherein said light source is a multiwavelength light source.

37. (currently amended)    The apparatus as claimed in ~~any one of~~ claim 28-36 wherein detection is effected using a plurality of source/detector configurations.

38. (currently amended) The apparatus as claimed in ~~any one of~~ claim 28-37 comprising a plurality of detector channels.

39. (currently amended) The apparatus as claimed in ~~any one of~~ claim 28-38 comprising a plurality of source channels.

40. (currently amended) The apparatus as claimed in ~~any one of~~ claim 28-39 further comprising wavelength selection means between said source and said object for selecting one or more excitation wavelength.

41. (currently amended) The apparatus as claimed in ~~any one of~~ claim 28-40 further comprising wavelength selection means between said object and said detector for selecting one or more emission wavelengths.

42. (currently amended) The apparatus as claimed in ~~any one of~~ claim 28-41 wherein said detector in a trans-illumination geometry operates in time domain, frequency domain or continuous wave mode.

43. (new) The method as claimed in claim 15 wherein said emission intensity is obtained in a modality selected from time domain, frequency domain and continuous wave.